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Grandma's Experiences Leave a Mark on Your Genes

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7–8 minutes

Darwin and Freud walk into a bar. Two alcoholic mice — a mother and her son — sit on two bar stools, lapping gin from two thimbles.

The mother mouse looks up and says, “Hey, geniuses, tell me how my son got into this sorry state.”

“Bad inheritance,” says Darwin.

“Bad mothering,” says Freud.

For over a hundred years, those two views — nature or nurture, biology or psychology — offered opposing explanations for how behaviors develop and persist, not only within a single individual but across generations.

And then, in 1992, two young scientists following in Freud’s and Darwin’s footsteps actually did walk into a bar. And by the time they walked out, a few beers later, they had begun to forge a revolutionary new synthesis of how life experiences could directly affect your genes — and not only your own life experiences, but those of your mother’s, grandmother’s and beyond.

The bar was in Madrid, where the Cajal Institute, Spain’s oldest

academic center for the study of neurobiology, was holding an international meeting. Moshe Szyf, a molecular biologist and geneticist at McGill University in Montreal, had never studied psychology or neurology, but he had been talked into attending by a colleague who thought his work might have some application. Likewise, Michael Meaney, a McGill neurobiologist, had been talked into attending by the same colleague, who thought Meaney's research into animal models of maternal neglect might benefit from Szyf's perspective.

Michael Meaney, neurobiologist. (Credit: Owen Egan/McGill University)

> "I can still visualize the place — it was a corner bar that specialized in pizza," Meaney says. "Moshe, being kosher, was interested in kosher calories. Beer is kosher. Moshe can drink beer anywhere. And I'm Irish. So it was perfect."

The two engaged in animated conversation about a hot new line of research in genetics. Since the 1970s, researchers had known that the tightly wound spools of DNA inside each cell's nucleus require something extra to tell them exactly which genes to transcribe, whether for a heart cell, a liver cell or a brain cell.

One such extra element is the methyl group, a common structural component of organic molecules. The methyl group works like a placeholder in a cookbook, attaching to the DNA within each cell to select only those recipes — er, genes — necessary for that particular cell's proteins. Because methyl groups are attached to the genes, residing beside but separate from the double-helix DNA code, the field was dubbed epigenetics, from the prefix epi (Greek for over, outer, above).

Originally these epigenetic changes were believed to occur only during fetal development. But pioneering studies showed that molecular bric-a-brac could be added to DNA in adulthood, setting off a cascade of cellular changes resulting in cancer. Sometimes methyl groups attached to DNA thanks to changes in diet; other times, exposure to certain chemicals appeared to be the cause. Szyf showed that correcting epigenetic changes with drugs could cure certain cancers in animals.

Geneticists were especially surprised to find that epigenetic change could be passed down from parent to child, one generation after the next. A study from Randy Jirtle of Duke University showed that when female mice are fed a diet rich in methyl groups, the fur pigment of subsequent offspring is permanently altered. Without any change to DNA at all, methyl groups could be added or subtracted, and the changes were inherited much like a mutation in a gene.

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Moshe Szyf, molecular biologist and geneticist. (Credit: McGill University)

Now, at the bar in Madrid, Szyf and Meaney considered a hypothesis as improbable as it was profound: If diet and chemicals can cause epigenetic changes, could certain experiences — child neglect, drug abuse or other severe stresses — also set off epigenetic changes to the DNA inside the neurons of a person's brain? That question turned out to be the basis of a new field, behavioral epigenetics, now so vibrant it has spawned dozens of studies and suggested profound new treatments to heal the brain. According to the new insights of behavioral epigenetics, traumatic experiences in our past, or in our recent ancestors' past, leave molecular scars adhering to our DNA. Jews whose great-grandparents were chased from their Russian shtetls; Chinese whose grandparents lived through the ravages of the Cultural Revolution; young immigrants from Africa whose parents survived massacres; adults of every ethnicity who grew up with alcoholic or abusive parents — all carry with them more than just memories.

Like silt deposited on the cogs of a finely tuned machine after the seawater of a tsunami recedes, our experiences, and those of our forebears, are never gone, even if they have been forgotten. They become a part of us, a molecular residue holding fast to our genetic scaffolding. The DNA remains the same, but psychological and behavioral tendencies are inherited. You might have inherited not just your grandmother's knobby knees, but also her predisposition toward depression caused by the neglect she

suffered as a newborn.

Or not. If your grandmother was adopted by nurturing parents, you might be enjoying the boost she received thanks to their love and support. The mechanisms of behavioral epigenetics underlie not only deficits and weaknesses but strengths and resiliencies, too. And for those unlucky enough to descend from miserable or withholding grandparents, emerging drug treatments could reset not just mood, but the epigenetic changes themselves. Like grandmother's vintage dress, you could wear it or have it altered. The genome has long been known as the blueprint of life, but the epigenome is life's Etch A Sketch: Shake it hard enough, and you can wipe clean the family curse.

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